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Disseminated lesions of the central nervous system in course of pediatric brain tumors

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Summary

Background: Neoplasms of the central nervous system (CNS) are, apart from leukemia, the most frequent malignant disorders in the childhood. Among the brain tumors, those of poorly differentiated cells – give metastatic lesions to the CNS. The aim of the paper was to evaluate the features of CT and MR images detecting dissemination of the primary brain tumors.

Material/Methods: From 1993 to 2005 in the Department of Radiology of the Polish Mother's Memorial Hospital – Research Institute, the disseminations to CNS were observed in 35 children who were previously operated for primary brain tumors. CT and MR examinations of the brain were performed in all patients (22 males and 13 females; age: 5 mo – 18 y) and MR imaging of the spinal cord was done in 18 children.

Results: Multiple metastases to the cerebral structures were detected more often (in 23 patients – 66%) as compared to single lesions. The most frequent disseminations were observed in patients with diagnosis of medulloblastoma – 13 children, PNET – 4 and pineoblastoma – 3 patients. Twelve children had single metastatic tumors (out of the primary neoplasm location): in the course of medulloblastoma – 6, and PNET – 2 patients. Eighteen MR examinations of the spinal canal showed disseminations of the brain tumors in 9 children; concomitant metastatic nodules in the brain were detected in 4 patients.

Conclusions: CT and MR imaging of the CNS enables evaluating the dissemination of primary brain tumors in children. Any asymptomatic progression of the primary neoplastic disease may be detected by means of control diagnostic imaging, which reveals the tumor spread. Especially in patients with medulloblastoma and pineoblastoma, the spine MR imaging with gadolinium is mandatory.

Key words: tumor dissemination • brain tumor • children

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Background

Tumors of central nervous system (CNS) are the second most proliferative tumors in children, after leukemia. Brain tumors occur as often in the supratentorial as in the subtentorial space, except for children in the first year of life or older than 10 years, in whom the supratentorial localization dominates. In patients aged 2–10 years most of the tumors are localized within the posterior cranial fossa [1, 2].

Among many histological types of brain tumors in childhood, two are dominant – pilocytic astrocytoma and medulloblastoma. The other frequently observed tumors are: ganglioglioma, ependymoma, supratentorial primitive neuroectodermal tumor (sPNET), disembryoplastic neuroepithelial tumor (DNT), craniopharyngioma [2].

The prognosis for patient with brain tumor depends on its histopathologic image, level of malignancy and on the

possibility of its complete surgical resection [1, 3]. Among the pediatric tumors, low malignancy neoplasms are more frequent (2/3 of cases). Tumors with high malignancy and poor prognosis include i.a. embryonal carcinomas (medulloblastoma, sPNET), anaplastic gliomas and pineoblastomas [4–6].

Very often, by the time of diagnosing the before mentioned tumors, the proliferative process had already occupied the subarachnoid space and blood vessels [7]. Therefore complementary treatment (radiotherapy, chemotherapy) is indispensable after the surgical procedure.

In imaging examinations of patients with tumors of high histological malignancy, we often observe neoplastic dissemination within the routes of cerebrospinal fluid flow. It can occur within various periods after the diagnosing (from 2 to 61 months), but it can be sometimes observed at the time of tumor detection [8]. The presence of dissemination at the time of tumor diagnosis dramatically worsens the prognosis, like in cases when this process occurs in a later stage of the disease. In case of medulloblastoma, the 5-year survival time of patients is twice longer for those without disseminations [6].

The aim of his study was to evaluate imaging techniques in diagnosing the neoplastic dissemination to the CNS in children with primary brain tumors.

Materials and methods

The imaging examinations of CNS of children with primary brain tumors carried out in 1993–2005 at the Department of Diagnostic Imaging of Polish Mother's Memorial Hospital (PMMH) in Lodz, revealed traces of dissemination in 35 patients. The patients were mainly boys (n=22) and they were aged 5 months to 18 years.

Table 1. Dissemination of the brain tumors in 35 children.

Type of tumor	Multiple lesions n = 23	Single metastasis n = 12	Total
Medulloblastoma	13	6	19
PNET	4	2	6
Pineoblastoma	3	0	3
Astrocytoma pilocyticum	1	1	2
Ependymoma	1	2	3
Germinoma	1	1	2

Children underwent CT and MR examinations of the head, repeatedly in many cases, with predominance of the MR. The diagnostics was extended by MR of the spinal canal in 18 cases. The frequency of check-up examinations after completion of surgical treatment depended on algorithms of oncological procedures for particular cases of malignant tumors, as well as on the clinical course of the disease.

Usually the first imaging exam was performed 3 months after the operation, the next – every 6 months for 2 years after the operation and the following – once a year. Clinical symptoms suggesting relapse of the disease were always considered as indications for imaging examination apart from the appointed date.

Results

The examined children were divided into two groups according to the morphologic image of the dissemination – single metastasis out of the postoperative site and multiple disseminated lesions (table 1). The latter were diagnosed more often – in 23 patients, including 15 boys. Patients in this group were aged 5 months to 13 years (median 7 years

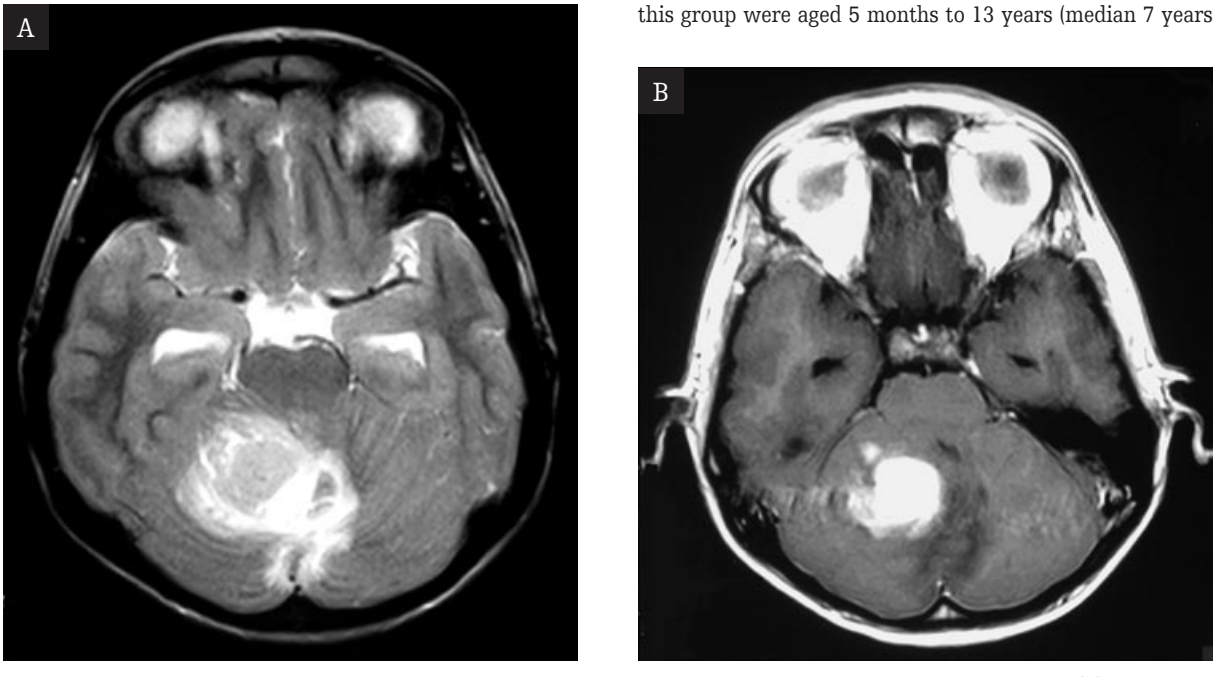

Figure 1. A metastatic lesion in the right cerebellar hemisphere after resection of the fourth ventricle ependymoma. Axial T2-weighted (**A**) and T1-weighted after paramagnetic contrast administration (**B**) image. Heterogeneous tumor displacing the right cerebellar hemisphere.

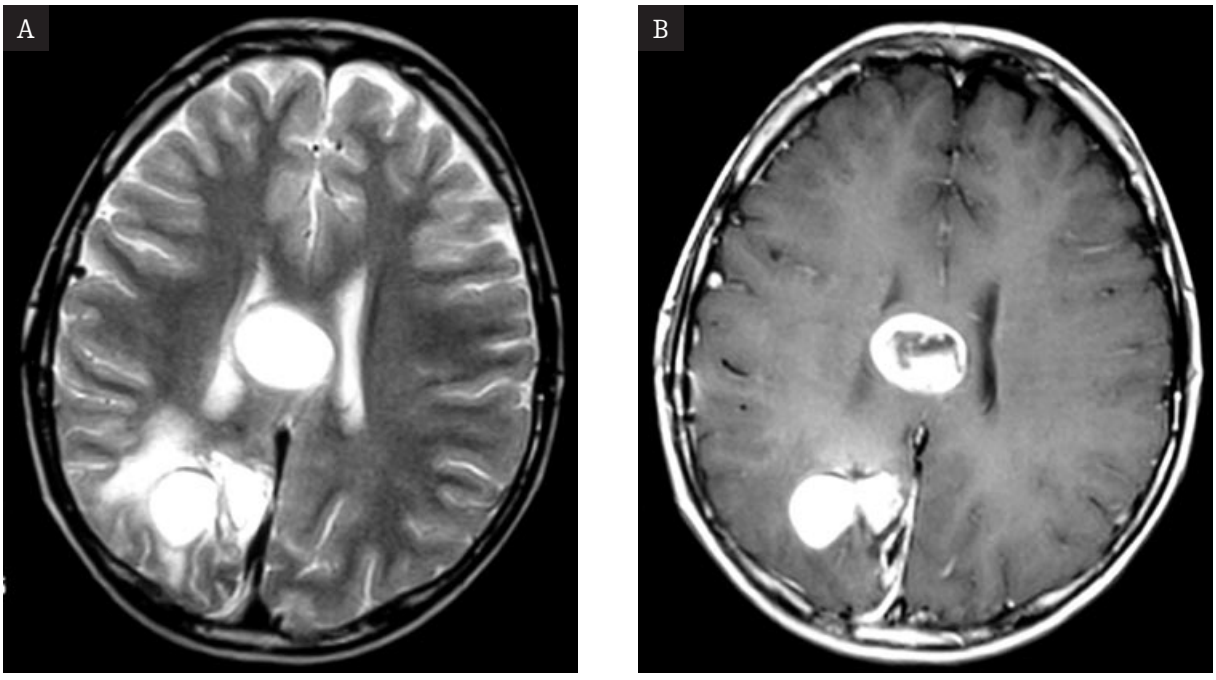

Figure 2. Metastases into the brain after the resection of pineoblastoma. Axial T2-weighted (**A**) and T1-weighted post-gadolinium (**B**) images. Metastatic mass in the corpus callosum and the second focus in the right occipital lobe. Edema of the deep white matter surrounding the brain tumor.

11 months). Patients with single lesions located outside the primary operative site comprised a less numerous group (fig. 1). There were 12 children, including 7 boys, in the group. Age of patients varied from 2 to 18 years (median 7 years 6 months).

In patients with embryonal carcinomas (medulloblastoma, sPNET) multiple lesions occurred twice as often as single metastatic lesions. In three patients with pineoblastoma only multiple disseminated changes were found. In two patients – one with medulloblastoma and the other with ependymoma, the relapse of tumor in the postoperative site followed by signs of generalized metastasis were observed. Single metastatic tumors occurred as often in the supratentorial as in the subtentorial space. Multiple changes occupied the whole brain in 16 of 23 cases, in 5 – the supratentorial space and in 2 – they occurred only within the posterior cranial fossa.

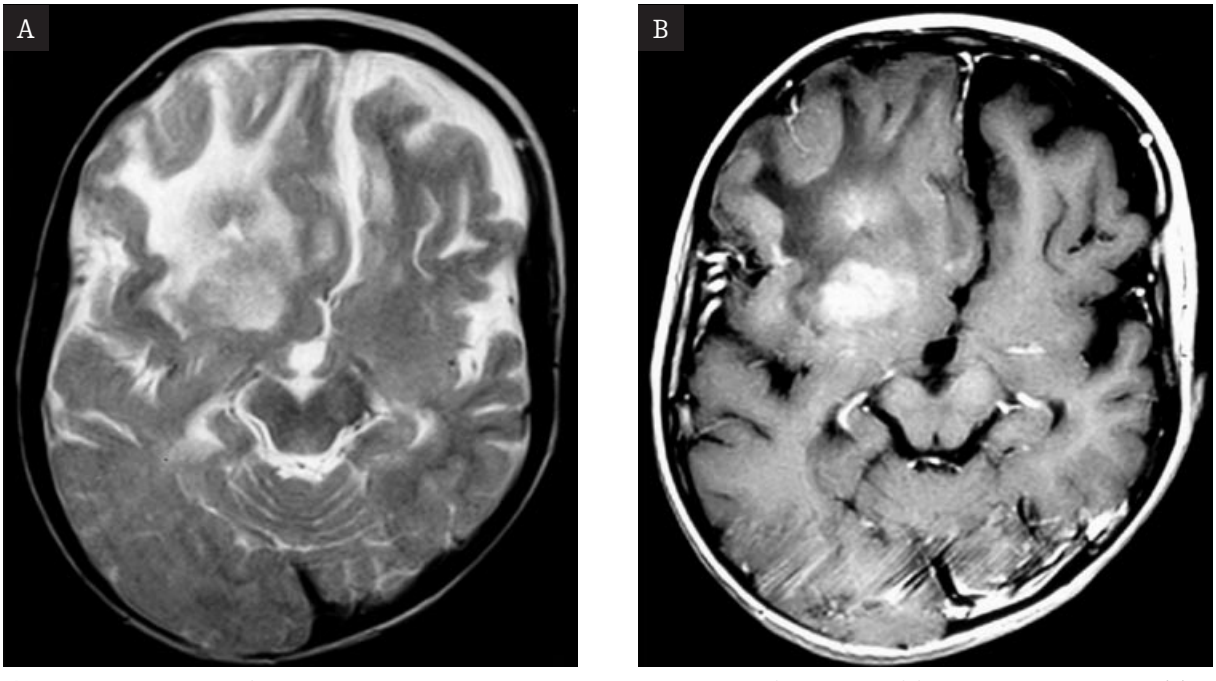

Figure 3. Frontal metastasis of the right cerebral hemisphere in a child with previous resection of the PNET in left frontal lobe. Axial T2-weighted (**A**) and post-contrast T1-weighted images (**B**) show mass with surrounding edema in the deep white matter of the frontal lobe.

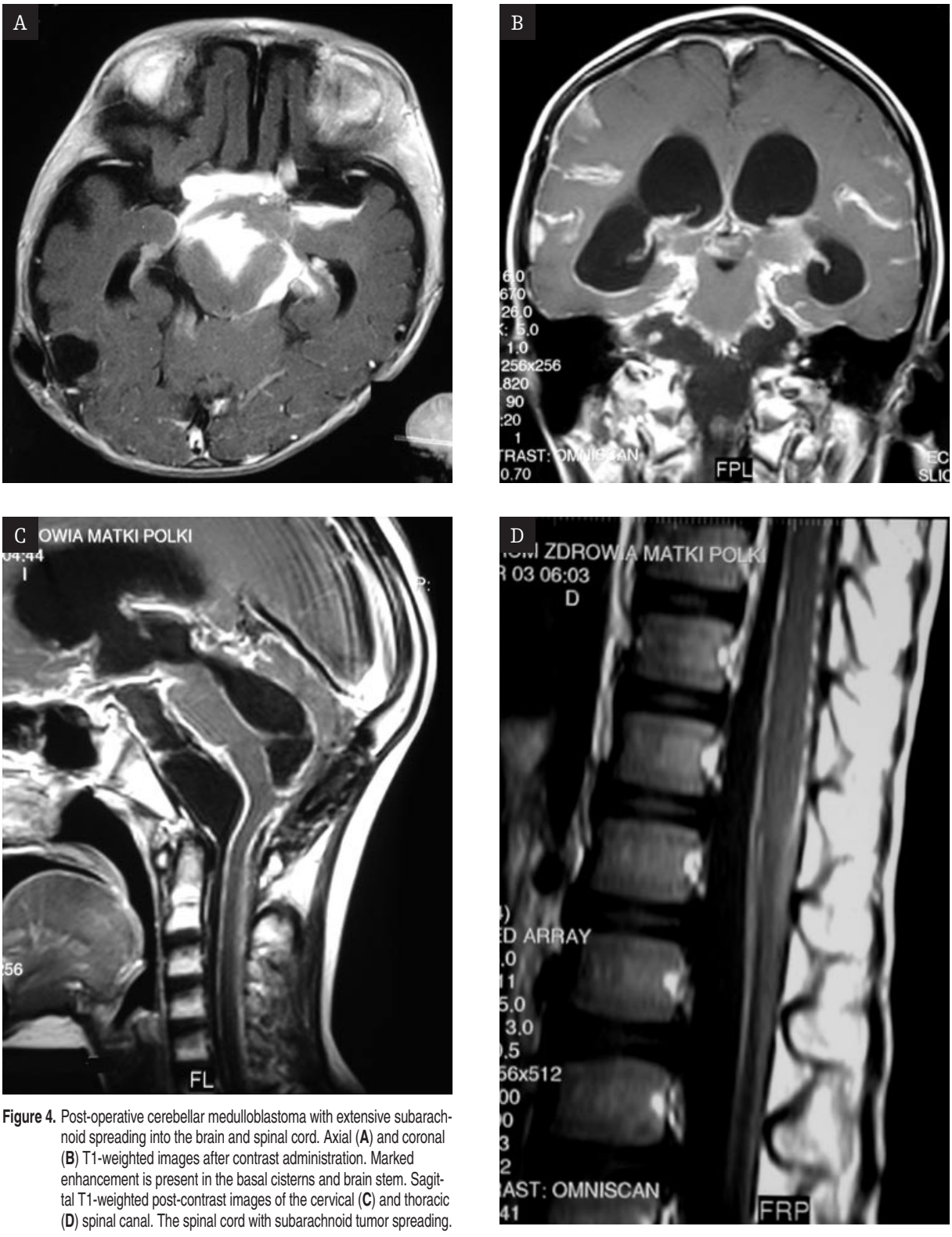

Figure 4. Post-operative cerebellar medulloblastoma with extensive subarachnoid spreading into the brain and spinal cord. Axial (**A**) and coronal (**B**) T1-weighted images after contrast administration. Marked enhancement is present in the basal cisterns and brain stem. Sagittal T1-weighted post-contrast images of the cervical (**C**) and thoracic (**D**) spinal canal. The spinal cord with subarachnoid tumor spreading.

MR examination of the spinal canal revealed metastatic focuses in 9 of 18 patients. Disseminated lesions within the spinal canal coexisted with multiple metastasis within the brain in 4 patients with medulloblastoma and in all 3 children with pineoblastoma. Moreover, dissemination to the spinal canal occurred in 2 patients with single metastatic tumors of the brain – in one child with medulloblastoma and the other with ependymoma.

In most cases, multiple metastatic lesions were diagnosed within the first month after the operation. In one child the dissemination of primary neoplastic process was not observed until the 9th year after the operation.

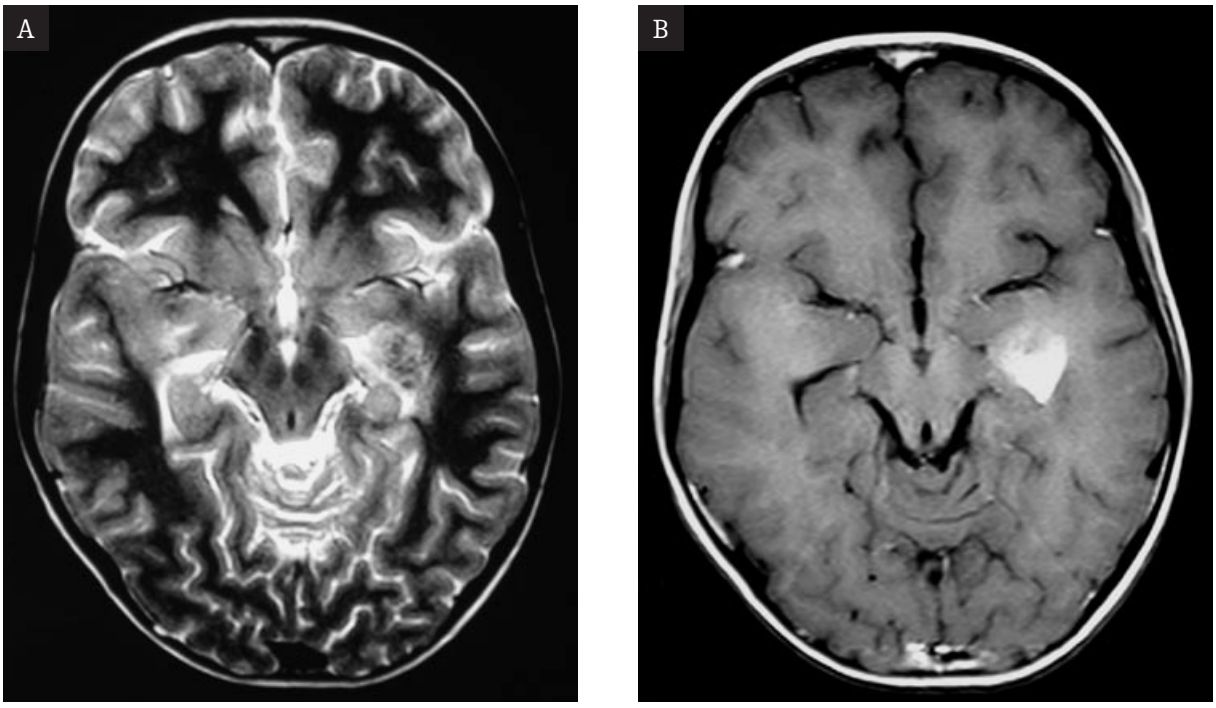

Figure 5. Metastatic lesion in the left temporal lobe of the astrocytoma observed after surgery of the primary tumor. Axial T2-weighted (**A**) and post-contrast T1-weighted (**B**) images. Heterogeneous tumor without peripheral edema of the brain tissue.

The average period of time between operation and the occurrence of multiple metastases was about 1.5 year. Single neoplastic metastases in the CNS were described after average 2–3 months after the operation of primary tumor – the earliest metastatic change detection was in the 4th month after the operation, while the latest was after 5 years.

Early multiple metastatic focuses occurred in patients with primary tumors in type of sPNET or pineoblastoma (fig. 2). Similarly, in the group of patients with early diagnosed metastatic lesions in form of a single tumor, the earliest metastasis occurrence was in a child operated for sPNET tumor (fig. 3).

Morphological representation of disseminated lesions in imaging examinations was characterized by multiple hyperdense nodules on CT images and hyperintensive on T2-weighted MR scans. These nodules covered not only the brain parenchyma, but also the subarachnoid space. Typical features of metastasis in course of medulloblastoma included metastatic focuses located subependymally in the lumen of ventricular system with associated widening of its lumen. Intensive enhancement of metastatic focuses was gained by means of intravenous administration of iodic specimen in the CT examination and paramagnetic contrast agent in MR scanning (fig. 4).

In children in whom the dissemination occurred within the spinal canal the metastatic focuses were seen in the MR examination as nodular changes, hyperintensive in T2weighted images, located in the spinal parenchyma and along nerve roots, in a typical form of a "falling drop". The morphology of these nodules was identical, regardless of the histological type of the primary tumor.

The distinctive features of single metastatic tumors in CT and MR examinations included solid structure in most cases (in 2 children – solid cystic) and location at the cortical-subcortical junction in brain. Moreover, they presented faint cytotoxic swelling of the adjacent tissues. After intravenous administration of contrast agent, considerably homogenous enhancement of tumor mass was visible (fig. 5). In two patients with single metastatic changes within the brain, in whom the occupation of spinal canal was also diagnosed, the studied lesions affected the lower segment of thoracic medulla.

Discussion

The presented group of patients with neoplastic dissemination to the CNS consisted mainly (almost 3/4) of children with embryonal carcinomas, medulloblatomas or sPNET tumors. Medulloblastoma of the cerebellum is the most common malignant brain tumor of childhood and constitutes 16–25% of all intracranial carcinomas [2, 4, 7]. The results of treatment applied to children with this kind of tumor suggest that features like child's sex, size of the primary tumor, duration of symptoms before diagnosis or completeness of resection are not significant prognostic indicators [6]. However, relapse in the place of tumor or occurrence of neoplastic dissection considerably shortens the survival time [4, 6]. Localization and character of the dissection results from the way the neoplastic process had spread by means of cerebrospinal fluid flow (ventricular system and subarachnoid space) [9]. The presence of neoplastic cells within the subarachnoid space results in disordered absorption of cerebrospinal fluid in the cerebral vault, what leads to hydrocephalus with accompanying clinical symptoms of intracranial tightness.

Early diagnosis of neoplastic dissection, especially in children with no clinical symptoms, is crucial. Prognosis for such patients is better than for children with dissemination with accompanying clinical symptoms. This observation relates to patients with medulloblastomas and patients with highly malignant gliomas as well [3, 4, 6]. Therefore, control examinations are significant for diagnosing the progress of sickness, also in the asymptomatic period. The protocol providing a certain frequency of check-up examinations, which is widely used in our institute, enables recognition of dissections in the group of patients, in which asymptomatic children constitute 70% [4].

Morphological character of the neoplasm recurrence in the analyzed group of children had the form of single metastasis, or more often – multiple dissected lesions. Neoplastic dissemination mostly concerned two histological types: medulloblastoma and pineoblastoma. This process is considered to be a characteristic feature of these carcinomas [1, 5, 6, 8–10]. It is estimated that in 14–43% of cases the spread by means of cerebrospinal fluid, usually to the spinal canal [5, 6, 10], takes place as early as at the time of medulloblastoma recognition [5, 6, 10]. This is why in many centres MR of the brain is performed together with MR of the spinal canal in order to find these lesions [10]. Barkovich claims that early, pre-operative evaluation of the level of advancement of neoplastic disease (staging) ought to be carried out due to the artifacts remaining in the MR examination of the spinal canal after the operation within the posterior cranial fossa. These artifacts hinder the unequivocal recognition of dissection [1]. If the advancement of medulloblastoma is evaluated postoperatively, full imaging of the spinal canal with the use of gadolinium is necessary [10]. It is obvious that detection of dissemination lesions based on imaging examinations is crucial for choosing the best treating method [4].

Conclusions

Diagnostic examinations of brain and spinal cord, especially the MR, enable the recognition and evaluation of the degree of advancement of the neoplastic dissemination in children with primary brain tumors of high histological malignancy.

Control imaging examinations of the CNS, performed in the course of treatment and after it, are indispensable for early diagnosis of neoplastic dissection during the clinically asymptomatic period.

In patients with medulloblastomas and pineoblastomas MR of the spinal canal with contrast agent administration is also necessary.

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